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EDITORIAL

EPIZOOTIC CEREBRO-SPINAL NEMATODIASIS OR SETARIASIS

SCIENTIFIC research is the key to the future. Medical knowledge advances by great leaps and bounds, and it is often so far ahead of any practical application that there are some who do not recognise its full value.

It can be likened to a great river which flows towards the sea. It is kept constant by the steady unfolding of basic knowledge, which simulates the springs at the source. At intervals, its volume is increased by discoveries, which disturb its surface to a limited extent, as does the influx of a tributary, but from time to time great discoveries explode upon us like a cloud-burst, the placid river becomes a torrent, old débris is swept away, and things which have been murky and obscure are clarified with great suddenness. When we think on these things great names come to mind — Pasteur, Lister, Pavloff, Ball, Sherrington and Hopkins.

Great discoveries bring great benefits, but they are not devoid entirely of danger. Their impact may attract such attention that other things suffer neglect.

The story of the last 100 years gives full example of this.

No one would deny the value of bacteriology to medical science, but, fortunately, there have been those who objected to it as an obsession. They continued in their own furrows, often lonely, often despised, but disheartened, never. Anatomists, physiologists, chemists and, not least, the parasitologists kept plodding away, steadily and modestly adding to the store of knowledge, and

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during the last 30 years, partly owing to the failure of the bacteriologists to live up to early expectations, they have come again into their own.

Anatomists and parasitologists in particular have done most valuable work, and we publish in this issue an account of work which bids fair to be as notable and revolutionary as any previous medical discovery.

The ætiology of some of the diseases of the nervous system has defied the efforts of our research workers for many years, and in consequence methods of prevention and cure have not been available.

The physician has been able to correlate the signs and symptoms, propound syndromes, and even give names to specific nervous complexes, only to confess that treatment was empirical.

Now, as the result of good team work between histo-anatomists and parasitologists, a ray of light is shed, and their work may lead to the opening of a new epoch in medical science.

The filaria worms of domesticated animals have been studied only superficially. A few years ago only the bravest of men would have ventured to suggest that they might invade the spinal cord. The filarioidea are unique amongst the nematodes so far as our present knowledge goes in that they have perfected a mechanism by which both their entrance to and exit from a host can take place through the skin. The life cycles of comparatively few species are known. Amongst those that are known there is relatively little variation, the microfilariæ produced by the adult female worm being taken up by blood-sucking arthropods in which, development of the worm to the infective stage takes place.

If the findings of Innes and his co-workers are substantiated, and we see no reason to doubt that such will be the case, for anatomists and parasitologists deal with facts and not conjecture, we may be at the beginning of a new era which will equal and surpass all those of the past.

GENERAL ARTICLES

EPIZOOTIC CEREBRO-SPINAL NEMATODIASIS OR SETARIASIS

focal encephalomyelomalacia in animals in the Orient caused by immature Setaria Digitata: a disease which may occur in animals in other parts of the world

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Introduction

THIS article, additional to a previous one (Innes, 1951), contains information on a "new nervous disease. The nature of it may interest those studying the nervous system from the point of view of pathogenic causes and effects. A consideration of the causal parasite (*Setaria*) may stimulate the veterinary helminthologist to probe more into its life cycle, and to resolve the complexities of filarial infestations in man and animals. Then, there is the question of the practical importance of the studies to the veterinary investigator, no matter what his specialisation is. The unfolding of the puzzle of the disease is an example of an oft-repeated story in veterinary medicine. Perhaps there are few really new diseases of animals (and there are none in which final clarification has been obtained), but in our journals there are a succession of papers delineating for the first time part of the natural history of a hitherto undescribed disorder. No disease entity, however, emerges through a preliminary phase of definition until someone finds it. This has often happened by luck, ingenuity, sometimes by brilliant direct observation, or by the development of some new clinico-pathological, or bacteriological, technique; more often it emanates from an assiduous study of diseased animals, and thereafter flourishes slowly by careful evaluation of clinical and pathological findings. In veterinary medicine perhaps particular emphasis might be placed on the latter, especially relating to nervous diseases. Without recognition of the essential lesion in nematodiasis, and its significance, many erroneous ideas might have arisen (and did—see Bush, 1951) and at present a pathological examination of the lesion is the only method of unequivocal diagnosis. It might serve as another object

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lesson. In work involving nervous diseases of animals, there has been a growing conviction that in the initial phase of pathological studies it is of paramount importance to examine the whole central nervous system quite systematically. Random, cheeseparing selection of tiny bits of tissue, especially in the length of the spinal cord, can arouse false impressions. Indeed, in setariasis such a procedure might have caused wrong conclusions of an absence of neuro-pathological changes. Because of the smaller size, and the less complex structure, of the brain of domestic animals, the veterinary pathologist is not faced with the same technical problem as his medical confrère. With modern histological techniques, whole coronal slabs of the animal brain can be cut (and embedded) from successive levels from the frontal poles to the medulla; if necessary the spinal cord can be cut through its length by transverse, alternating with longitudinal, slices, and the total number of blocks is not enormous. There is then no limit to topographic search for lesions, but unless this is performed answers may not be forthcoming to many questions raised by the clinical history of nervous disorders.

This paper focuses attention on first-class work in animal pathology done by Japanese veterinary pathologists and parasitologists — all unfortunately obscured because of World War II and of publication in the Japanese language. There may be specticism regarding the conclusions on nematodiasis, for it takes a long time before pathological information on " new diseases " is accepted. The history of veterinary medicine, however, has shown how often several diverse pathological conditions have been segregated from what was previously a supposedly, single, clinical syndrome. No one should now doubt* the visual evidence that the catastrophic damage to parts of the brain and spinal cord is the basic, structural alteration underlying " lumbar paralysis." In the opinion of one of us (J.R.M.I.), the work of the Japanese investigators has been of a superlative nature, marked by an appreciation of the value of pathological studies as well as the experimental method. An answer to all questions has not yet been obtained, but their studies can stand as a basis for future work by veterinarians in other parts of the world. All data point to the existence of a jig-saw problem of a disease, with a widely scattered global incidence, in which most pieces fit neatly into place in virtue of the Japanese work. There are

* A paper by Bush (1951) has created very erroneous ideas on " lumbar paralysis." It is vital to stress this, because of the repercussions arising now on method of control, and the future course of research in countries other than Japan (Ceylon and even the U.S.A.). Bush contends that there was really no entity such as enzoötic nervous disease in Japan caused by immature nematodes; the condition was essentially nutritional paresis—mineral deficiencies and osteomalacia. His exposition is a muddled one and it is difficult to disentangle original work from facts related to him by others. He seems to have been totally misinformed on previous Japanese work, to have been unaware of the neuro-pathological studies, and (perhaps because of language difficulty) the Korean Report and other Japanese papers cited by us are not mentioned. In the field no doubt (just like swayback in England at one time) lumbar paralysis was a clinical hotch-potch, *but* the keystone of any investigational survey (such as this of Bush) should virtually centre around paramount pathological study, and our paper indicates how meticulous these requirements might be. It is thus important to note how pathology was ignored by Bush, for if such studies had been made, a different story would have been revealed. The recommendations regarding control thus become somewhat puerile; his survey is a good example of the superficial limits of clinical and field studies of any animal disease—without pathology.—J.R.M.I.

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repercussions which cannot now be ignored, for they may have medical, as well as undisputed veterinary, importance.

Chronological Developments in Identification of the Disease

Emoto (1927) first recognised a form of "lumbar paralysis" in goats imported from Switzerland into Japan. Over 40 cases were studied. (This feature of an apparent greater susceptibility in imported stock arises repeatedly, and may still be an important factor in pathogenesis, i.e., indigenous animals may have more immunity.) The disorder occurred with seasonal, enzoötic regularity in the late summer and autumn. Young and adult animals were mainly affected, becoming paralysed in all four limbs, or only in the hind ones; the onset and course was acute, or subacute and more insidious. The pathology was designated to be lymphocytic meningitis with cerebrospinal malacia, but unfortunately the lesions were not illustrated and exact comparisons are now impossible. All circumstantial evidence indicates that the investigations in Japan and Korea since 1939 have been concerned with this same nervous disease.

Crawford (1939-42)—unaware of Emoto's work—studied lumbar paralysis of goats in Ceylon, which he recognised to be seasonal in occurrence; he showed that it was non-transmissible to laboratory animals or goats, that bacteria could not be identified as causal organisms, and that it was unproven to be due to poisonous plants. Innes (1951) thought that the probability of it being an avitaminosis was dubious postulation. Further field studies by Pillai, Mahamooth, and Malkani (1949) confirmed Crawford's data, and they recognised it in a variety of breeds of goats in Ceylon, many imported from India. They considered typical cases developed motor weaknesses and ataxia in the hind limbs only (or in all four), leading to swaying, tumbling, complete paralysis, and there was nystagmus occasionally. The onset was sometimes dramatically sudden, or it was subacute. The disease was non-febrile, and with no other constitutional signs. Most animals died, but a few recovered with minor, residual, limb weakness and impaired gait. By a study of material (provided by Pillai *et al.* [1949], sent from Ceylon), Innes (1951) identified the pathological nature of the disease. It was considered to be a focal, discrete, form of necrotising encephalomyelitis (or malacia), with an apparently haphazard distribution of the lesion (or few lesions) in the brain and cord. It was a unique type of structural change, distinctive from any other clearly pictured in domesticated animals up to that time. Some reference was made to a possible comparison with some human cases of subacute necrotising myelitis, or of eosinophilic meningitis, or of so-called multiple degenerative softenings. Existing information provided no clue as to cause (except in a negative sense by Crawford's work), and, except for the records of Emoto, there was no other described nervous disease of goats which required consideration. (In the caprine species, indeed, there has been a strange paucity of nervous diseases described, which include only listeriasis, tick-fever, inherited malformations, and a form of *myotonia congenita* [identical to Thomsen's disease of man] in the U.S.A.—see Innes, 1951.)

It is unlikely this position would have been altered soon except by the accidental discovery of new facts, in virtue of correspondence, between two of us (Innes and Shoho, on the unrelated subject of cerebellar atrophy) from which the present issues now arise. From 1939 onwards a tremendous amount of research was done by many Japanese investigators in Korea and Japan, concerning a seasonal enzoötic paralysis in sheep, goats, and horses. Most of the results were unfortunately published in Japanese, in a Special Korean Research Commission Report (1939-43, in five volumes). The names of the Japanese who have contributed include Niimi, Kimura, and 29 others.* A few papers have appeared with German summaries which give brief descriptions of some of the findings, viz., Yamagiwa and Shoho (1944), and Tanaka, Suu, Shoho, and Yamagiwa (1945). All facets of the problem as revealed by all these publications, by pathological studies of the disease in Japan and in the Ceylonese goats, by other experiments, and by bringing together relevant medical and veterinary literature dealing with unsolved nervous diseases, are dealt with below.

The Kind and Distribution of the Lesions in the Nervous System

There is no fundamental qualitative difference in kind, of the typical lesions in either the disease of sheep, goats, and horses in Japan (and in sheep and goats in Korea) on the one hand, or that of the goats in Ceylon on the other. Sections of all have now been studied by us. We can thus deal with the lesion as a unity, irrespective of anatomical location, of species, or of country of origin of the animal. It is advisable to emphasise that we are not dealing with a curious and rare disorder, but one which has occurred annually for many years in Japan and Korea (and Ceylon), as a seasonal enzoötic or even epizoötic of some severity. The total cases which have been examined by autopsies by the Japanese (and the disease diagnosed) now number many hundreds,† while the goat cases from Ceylon have been 8 (plus others recently studied by McGaughey (1951).

In most cases only a single lesion is found, in some there may be two or three, and only in a few are there more. Foci may be found anywhere in the central nervous system, and from this we have the impression of a very haphazard wandering of the immature worm once it reaches the craniovertebral canal. There is a total disregard by the parasite for neuro-anatomical landmarks, for structural boundaries, for meninges and vessels; yet time and again in Japan it was noted (by Yamagiwa, Shoho, and others) that the cervical cord and the thalamus were favoured sites, but many other regions have been a locus for damage. In the goats from Ceylon, the lumbar cord was involved three times; the cervical cord three; and in two, lesions were found in pons, cerebellum, or

*There were three chief groups of workers: one in Korea composed of members mainly from Pusan Serum Institute for Animal Diseases; one from the National Institute for Epizoötics (to which Dr. S. Ishii belonged); and one from the Institute for Infectious Diseases, University of Tokyo (to which Dr. Yamagiwa, Dr. Shoho, and Dr. Tanaka belonged).

†This figure does not reflect, however, the severity of the disease in some years in some localities, for in Fukushima out of 100,000 sheep about 6,000 have been stated to suffer from this nervous disorder.

mid-brain. The fortuitous distribution of foci harmonises with some of the reported clinical findings, i.e., with a variety of neurological signs indicating motor weakness, ataxia and paralysis of the extremities (and occasionally nystagmus), and with the fact that some animals may recover. Clearly, a small lesion of the variety described, and located in the lower lumbar part of the cord, would be less serious than one at a higher level of the brain stem and so on. Further, as the dimensions of the malacic lesion are approximately the same in sheep, goat, or horse, it might not produce such marked neurological signs in an animal with a more voluminous nervous system such as the horse* (cf. also later mention on " wobblers " in the U.S.A.).

Unless the lesion is hæmorrhagic, and this would depend on the circumstance of the parasite striking main vessels, the accurate detection of change by macroscopic examination (certainly of fixed material) might be difficult. With hæmorrhagic softening the task becomes easier, subsequent to slicing of the fixed brain and cord. In the end it was found necessary (by J.R.M.I. in the Ceylon cases) to embed the entire nervous system for section cutting. Coronal sections were thus made of the brain of the goats about every 5 mm. level, while transverse cuts were alternated with longitudinal ones of the cord; after examination of representative sections, further (even serial) preparations were then made from any desired block where a lesion was suspected. The Japanese workers, however, relied in the first place on macroscopic examination by making about 50 thin transverse cuts of brain and cord, when milky streaks and spots might be seen.

Apart from a solitary malacic lesion (or more than one), the remainder of the entire nervous system is normal, and areas only a few millimetres away may reveal no damage except for the secondary degeneration dealt with later. Thus one striking feature is the restricted irregular boundaries of the focus. All lesions seem to have a direct tracking from the pia inwards, although this may only be evident in serial sections. Cellular infiltrations in the meninges are constantly present but variable, may contain lymphocytes and polymorphs while eosinophils are fluctuating in numbers, but are sometimes predominant. This infiltration may be in epidural, subdural, leptomeningeal tissue, and around nerve roots, and may extend well away from the malacia. (Fig. 1 *a* and *b*.) Meningeal reaction might be an excellent guide for a further search for the central lesion if that is not found initially; it might also be misleading, for after a random choice of portions of the nervous system it might suggest that only such a selective meningeal process was present.

Hæmorrhage is variable, and as indicated might be absent. Under the low power there is an appearance of cracks and crevices, although some of this might be exaggerated by falling-out (see Fig. 1, Innes, 1951; and Fig. 7, Yamagiwa and Shoho, 1944). In a fully-developed lesion, and this may take only a few days (or even one day—in a case of Shoho's with pontine cavitation),

* The first observation on neural nematodiasis in young horses—with paralysis—in Japan was that of Oguni (see Itagaki); later Tanaka *et. al.* (1945) found cerebral lesions (some with parasites) in old serum horses in which the nervous system was systematically examined. These animals showed *no nervous symptoms*.

it is one of acute softening (a *status spongiosus*)—in which not only the myelin disappears, but all structures including ground substance — leading to micro-cavitation (Figs. 2 and 3). *Gemästete Glia* may be abundant in softened areas (Fig. 3 *a*), or involving vessels which in, and around, the lesion show extra-adventitial cellular cuffs and sleeves composed of a mixed collection of cells, and eosinophils may also be numerous. A salient feature to which attention is immediately drawn concerns the axis cylinders. In all areas close to the focus of softening there are irregular, homogeneous (sometimes faintly granular), globose bodies, faintly stained by cytoplasmic stains, unstainable by lipoid or myelin stains, but with affinity for any of the metallic impregnation methods used for axis cylinders (or glia). Some might be two to three times the normal diameter, but others are gigantically enlarged (Fig. 2 *b, c, d*). Any doubts that these are axis cylinders disappear if longitudinal sections are made (Fig. 2 *e*), for all stages can be seen from delicate to gross beading, to complete fragmentation, all occurring subsequent to the severance of the nerve fibres in the malacia. A bizarre collection of corkscrew spirals, glomerular balls, collateral excrescences, and varicose beadings may be found even in one field (Fig. 2 *c*). Further, particularly in the cord, if a series of sections are made above and below the malacic focus these axis cylinder swellings can be traced in an ascending and descending direction (see Text Fig. 1). At some levels this secondary degeneration may be the only histological change,* and isolated swellings, without any reaction around, are a pointer determining the need for a further search for real malacia.

Serial sections reveal that the malacic focus, with or without micro-cavitation, may be small in its widest transverse diameter, but tortuous in its wandering in any direction—in the cord often obliquely longitudinal. It starts in the subpial zone, straggles into the white matter of the cord, or the grey matter of the brain as the case may be, and it may penetrate quite deep. It may suddenly end in apparently normal nervous substance; on the other hand, a tracking from the *pia* in and out of the nervous tissue was seen by Niimi and Kimura (Korea) and by Yamagiwa and Shoho (Japan) many times, as well as by us in the Ceylonese goats. The focus may also cavitate beyond microscopic dimensions (see Fig. 3, Yamagiwa and Shoho, 1944).

Other histological features do not concern us in this paper, and have been dealt with by Innes (1951). It is manifest, however, that the extent and nature of the damaged white (and grey) matter is such as to be incontestably responsible for a paralytic disorder in a living animal, and that the variability —in anatomical location and severity—of the focal malacic process dovetails in with the diversity of the clinical signs noted in different living cases.

The Nature of the Nervous Lesion : A Comparison with Experimental Trauma, Compression Myelopathy, and Wallerian Degeneration

From the pathology alone many deductions can be made. Firstly, the lesion has no resemblance to that of any of the established disseminated encephalitides caused by viruses, nor to the more suppurative or granulomatous

* See later reference to wobblers in foals (Olafson, 1942) and Fig. 5 of his paper.

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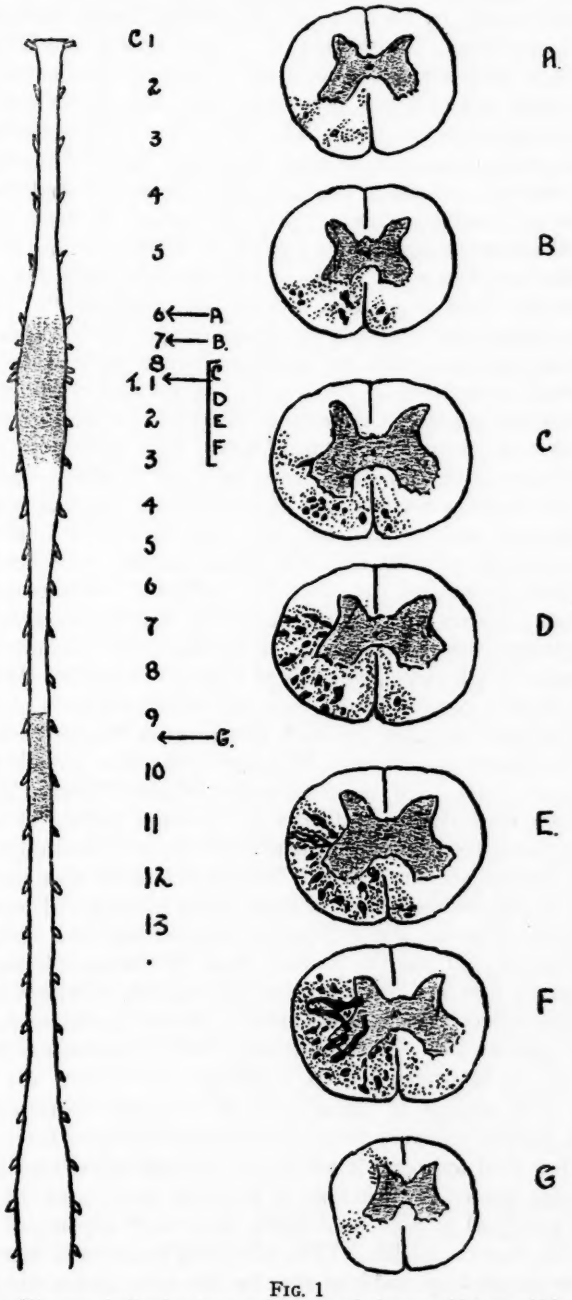

FIG. 1

Nematodiasis.—Diagram indicating type and extent of change which would be seen in sections cut above, below and through a malacic focus in the cord. On left, diagram of spinal cord with segments numbered. On right, transverse sections—the dots represent secondary degeneration and the black areas—foci of softening. Compare this with experimental trauma in the cord (Fig. 4a-d).

types of lesions caused by bacteria such as Listeria, nor to protozoan diseases (caused by *Toxoplasma, Histoplasma,* or *Trypanosoma*), nor to any mycotic condition. It is obviously not a focal demyelinating disease (*per se*), for all structures (myelin, axis cylinders, nerve cells, and glia) disintegrate and become liquefied in the centre of the focus. The disease is not a systematised one.

Whether we consider one, or more than one, lesion in the same animal, it is patent that the process is one following relatively rapid destruction of nervous tissue in a restricted track. Normal structure in the centre of this is completely obliterated as liquefactive necrosis is initiated to form irregular areas of micro-cavitation—hence the cracks or crevices seen under low power (or—as Yamagiwa described it—"*Höhlen- und Spaltenbildung*"). Some of the inflammatory sequel must certainly be related simply to this tissue destruction and perhaps nothing else, unless the immature worms produce an irritant toxic substance (which is unproven). The swellings of the axis cylinders, which lend to the composite lesion such a characteristic diagnostic feature, require emphasis. In consideration of the demyelinating diseases, it is traditional that in these (the classical example being multiple sclerosis) there is selective lysis of myelin followed by the irregular swelling and fragmentation of the axis cylinders. This beading is fine and varicose, and has been illustrated since Charcot's time in the lesions of multiple sclerosis, and other demyelinating conditions. However, in none of these do we find the enormous, ballooned swellings and distorted, fragmented axis cylinders as is seen in nematodiasis. Further, a search of textbooks on neuro-pathology does not reveal any illustration of this feature of a malacic lesion (traumatic or otherwise), which is so striking. Doubtless they have often been seen in human nervous lesions, but they may have been glossed over or they may have been mistaken for such structures as myelin balls or *corpora amylacea.* An answer can, however, be found if reference is made to Wallerian degeneration (see Cajal, 1928, on degeneration of nerve fibres). Since Waller's day it has been illustrated in textbooks by drawings mainly of experimental lesions in peripheral nerves, never in neuro-pathological literature by figures of lesions in the central nervous system. The observation is thus an ancient one, and probably is well known outside of print and is in danger of being forgotten. All this evidence, however, was sufficient to support our view that, irrespective of cause, the lesion itself was the primary result of trauma. If this were so, it was contemplated that the concept should be capable of experimental proof, and that further analogies should be found in cases of spontaneous, mechanical trauma to the spinal cord. These phenomena were demonstrated by one of us (J.R.M.I.), and are illustrated in Figs. 4 and 5.

Experimental trauma to spinal cord in a sheep.—With local procaine anæsthesia, a lumbar puncture needle was inserted between L.2-3 in an adult sheep, and after fluid appeared it was thrust into the spinal cord and wiggled. There was some immediate twitching of the hind limbs, and the animal was precipitously paralysed in both hind limbs, with more hypotonicity of muscles on the right side than on the left. (The lesion was found to be more unilateral.) The sheep was propped up, and kept alive for five days, during which time it ate

and drank normally, showed no ill-health other than inability to rise on its hind limbs (i.e., there was complete, posterior, flaccid paralysis). The animal was killed, and the entire central nervous system taken and fixed in formol-saline before slicing. There was no hæmorrhage visible either in the meninges at the site of the traumatic puncture, or in the cord. A minute discrete focus of greenish-yellow malacia was found between L.2-3 which faded out rapidly in an ascending and descending direction. Eighteen separate blocks were cut from the cord, most of these immediately above and below the macroscopic focus, but some from C.1, C.7, T.12, L.5 and L.6. Detailed descriptions of the findings are needless, for they are apparent in the figures with their legends; a traumatic lesion was produced, which in most ways duplicated that in nematodiasis. In the centre of the focus there is complete disintegration of white matter (and grey), marked leucocytic infiltration, but no eosinophils, around vessels as well as in a scattered way, *gemästete Glia* (filled with lipoid) abounded, and gigantic axis cylinder swellings formed a dominant feature. The swellings could be followed in an ascending and descending manner in tracts for about 1 to 2 cmm., but no farther. There was no marked secondary degeneration, or other change, found in the ventral or dorsal columns of white matter in T.12, or in L.6 with ordinary stains, and, as the figures show, at a shorter distance from the focus only a few axis cylinder swellings were noticeable.

Other figures (Fig. 5) demonstrate lesions in a spontaneous case of compression myelopathy in a dog. This animal had no definite history of accident, nevertheless it developed dramatic, sudden, complete, flaccid paralysis with loss of sensation of the hind limbs and retention of urine, and was killed *in extremis* on the third day. Apart from a gangrenous cystitis, there was an extensive, complete, transverse softening of the spinal cord about L.3; although hæmorrhage was found in lumbar muscles no vertebral fracture or spicules of bone were found, and the cause was undetermined. The figures show the necrotising, liquefactive type of damage through the centre of the lesion, and evidence of secondary degeneration in persisting tissue below the focus.

Clearly and distinctly, therefore, there is evidence that the ætiology of the animal paralysis might possibly be linked with some factor, which could be simulated by experimental trauma or in the early stages of a compression myelopathy. Further, in all these conditions the presence of axis cylinder swellings, standing isolated in the cord (or brain) away from any malacic focus, might be a guide in determining the actual site of severance of nerve fibres. In animals, in both Japan and Ceylon, the clinical evidence indicates that in some cases of nematodiasis recover, with a little residual motor impairment. An insufficient number of these cases has been studied by the Japanese, but Yamagiwa defined the lesion in such healed cases as one of sclerosis, and it is hoped to reproduce this experimentally by trauma. (Small cerebral foci of sclerosis were also found in the old serum horses, which showed no nervous symptoms, by Tanaka *et al.*, 1945.)

It was concluded that the available pathological knowledge supported the concept that the focal malacia in " lumbar paralysis " was caused by traumatic

damage, which could ostensibly be inflicted mechanically on nervous tissue simply by the entry and wandering of a young worm.

The Cause of Lumbar Paralysis—Cerebro-spinal Nematodiasis

The cause of the disease in sheep, goats, and horses was established by the Japanese to be immature *Setaria digitata*, from a study of natural cases followed by the crucial method of experiment. A full account of the work in sheep and goats is given in the Special Korean Research Commission Report (1939-43),* while some further experiments on horses are given by Itagaki *et al.* (1947) and on goats by Ishii (1951).

Setaria digitata (von Linstow, 1906, Rail. & Henry, 1911, synonyms *S. cervi* [Rud., 1819], Baylis, 1936), *S. labiato-papillosa* (Perronc., 1882, Rail. & Henry, 1911) is a filarial worm, the natural host of which is cattle, in which it lives in the peritoneum without producing any apparent pathogenic effect (Cameron [1934] depicts a small peritoneal tubercle-like lesion). Most textbooks on parasitology (e.g., Cameron, 1934; Mönnig, 1941; Chandler, 1949) admit of ignorance concerning the life cycle of this species (as well as the others, viz., *S. equina* and *S. marshalli*), particularly regarding their pathological significance. Their complete range of hosts is uncertain, but they produce living microfilariæ and an intermediate host vector (mosquito?) is always necessary. Altogether these species might appear to have an almost ubiquitous distribution throughout the world, certainly in the Orient (including Ceylon and India). According to Cameron none have been identified in Britain, but *S. digitata* is a common parasite of cattle in the United States (Dikmans—personal communication), and Chandler states that *Stomoxys calcitrans* is also an intermediate host, which may be of importance from the point of view of the occurrence of the disease in the U.S.A. or elsewhere.

No great search has been made of British and American parasitological literature, but Baylis (1939) gives a little more information. According to him the female *Setaria equina* is viviparous and produces sheathed microfilariæ; the adult worms inhabit the peritoneal cavity (chiefly of ungulates); the microfilariæ in the blood measure about 0.28 mm. in length and 7 microns in thickness (Fig. 7 *a*). No information is given about pathogenesis. In view of what is mentioned later about worm-in-the-eye of horses, it is significant historically that the worm was called *Filaria oculi* nearly 100 years ago. *Setaria digitata* (synonym of *S. cervi*), which may have been confused sometimes with *S. labiato-papillosa*, seems to be recognised as a widely distributed parasite in cattle (and other *bovidæ* and *cervidæ*) and inhabits chiefly the peritoneal cavity. The male measures 30 to 60 mm. long, about 0.35 to 0.5 mm. in thickness, female about 40 to 120 mm. by 0.5 to 0.86 mm., but no measurements are given for microfilaria in the blood (Fig. 7 *b*) and nothing is noted about pathogenesis. The Japanese workers have filled many of the gaps in the life history and helminthology, and it is hoped a separate publication in English will appear on this by various workers.

* A full English translation of which has not yet been made.

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LEGENDS TO MICROPHOTOGRAPHS

FIG. 1

Nematodiasis, goat, Ceylon. Spinal cord.—Showing meningeal infiltration in (*a*) epidural tissue, and (*b*) around nerve roots; many polymorphs and eosinophils were present. H.E. × 200.

FIG. 2

Nematodiasis, goats, Ceylon. Spinal cord.—(*a*) Area at almost extreme margin of lesion in ventral column of white matter of cord (ventral fissure and central canal shown) showing small area of liquefaction, microcavitation, and some cellular infiltration around, and tracking in from *pia*. (*b*) Another area from same cord nearer centre of lesion, showing liquefaction and cavitation, scanty swollen axis cylinders. (*c*) Same case through centre of focus of malacia with gigantic swollen axis cylinders; H.E. × 400. (*d*) Another case showing some perivascular cuffing in an area of softening; H.E. × 200. (*e*) Same case as 2(*c*) showing a grossly swollen and beaded axis cylinder in longitudinal section; H.E. × 200.

FIG. 3

Nematodiasis, sheep, Japan. Mid-brain.—(*a*) Showing an area of softening with massive *gemästete Glia* formation; H.E. × 100. (*b*) A malacic focus with an identical appearance to 2(*c*); H.E. × 200.

FIG. 4

Experimental needle-puncture traumatic malacia. Sheep.—Figs. 4 a-c on left are low-power photos of ventral columns of grey and white matter with central canal on left and ventral fissure parallel to bottom. In (*a*) there is enormous damage to grey and white matter with liquefaction and microcavitation and much inflammatory cellular infiltration; the intensity lessens from a-c, the sections having been cut at approximately 2 mm. from each other below the centre of the focus which was in L2-3. In (*c*) secondary degeneration is prominent in the ventral columns and in (*d*) there is scarcely any evidence of histological damage. Figs. 4 a-d on the right are high-power photos of typical areas and show the severe malacic process in (*a*), ballooned myelin sheaths (spaces) with enormous swollen axis cylinders in (*c*), and only an occasional swollen axis cylinder in (*d*). All H.E. × 100 and 400.

FIG. 5

Compression myelopathy, natural case, dog. Lumbar spinal cord.—Three days' history of complete posterior flaccid paralysis. Ventral column in (*a*) showing the severe necrotising type of lesion with destruction of myelin sheaths and axis cylinders, while in (*b*) high power of edge of lesion shows an appearance in parts like 4(*c*). H.E. × 100 and 400.

FIG. 6

Nematode larva in spinal cord, experimental (by courtesy of von Brand and Cullinan, 1943).—(*a*) Chicken artificially infected with *Eustrongylides spp.*, paralysis and death in 24 hours; longitudinal section of spinal cord showing cross-section of larva compressing and indentating the cord. (*b*) Rat similarly infected, with paralysis and death in three days; transverse section of cord with larva. H.E. × 100.

FIG. 7

Microfilaria.—(*a*) *Setaria equina*, blood; horse, U.S.A. (*b*) *Setaria digitata*, blood; cattle, Japan. Compare size. Baylis gives measurement of *S. equina* as being 0.28 mm. by 7 microns in thickness. Blood hæmolysed and stained H.E. × 200.

FIG. 8

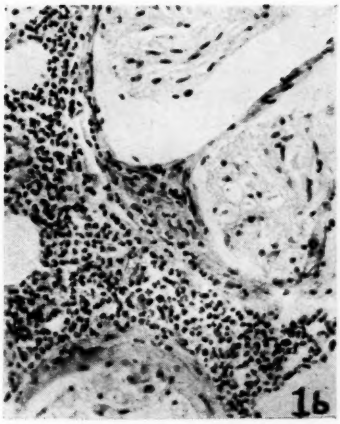
Setaria digitata.—(*a*) Mosquito-stage larva, unstained × 50, harvested at 14 days (photo by courtesy of Dr. S. Ishii, Tokyo). (*b*) Transverse section of nematode dissected from cerebral malacic focus in equine case by Dr. Tanaka, × 400. (*c*) Transverse section of nematode in centre of malacic focus in spinal cord of sheep case, H.E. × 90. (*d*) Goat case, Japan, H.E. × 200. (*e*) Nematode cut obliquely in section of cerebellar lesion, sheep, Japan, H.E. × 90.

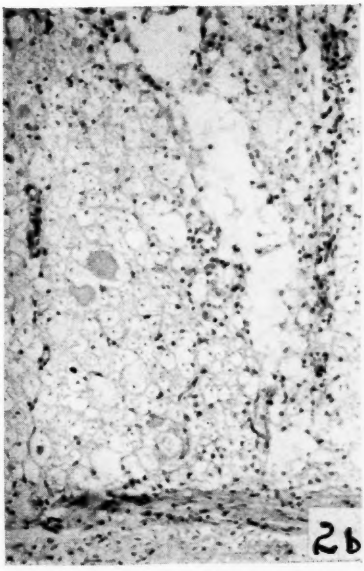
FIG. 9

Caprine nematodiasis, Ceylon.—Coiled body with a hyaline capsule found at the centre of a granulomatous focus within the cervical spinal cord. There is little doubt that this is an immature nematodes. H.E. × 620.

XUM

PLATE I





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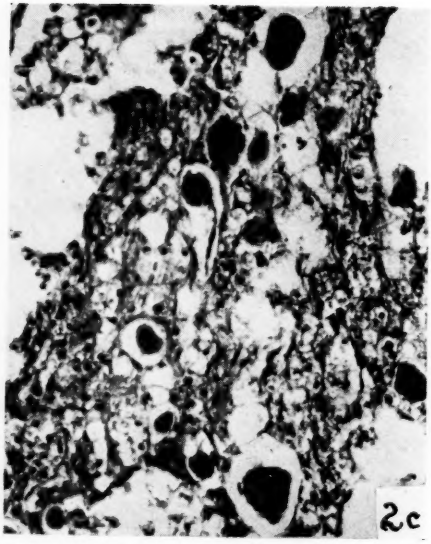
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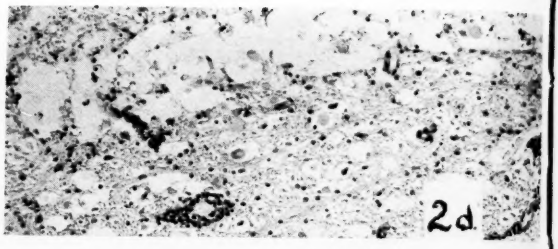
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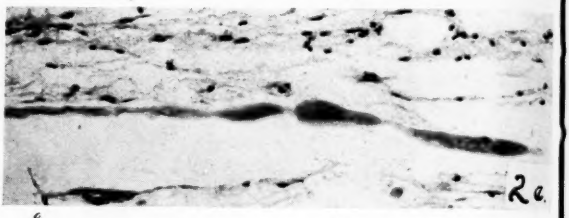
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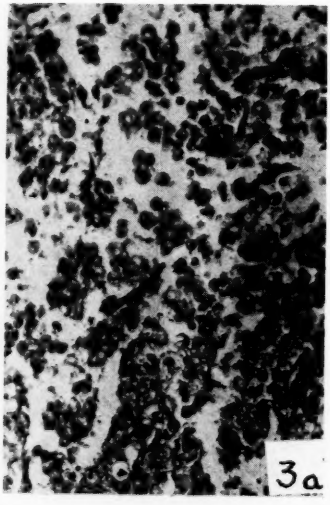
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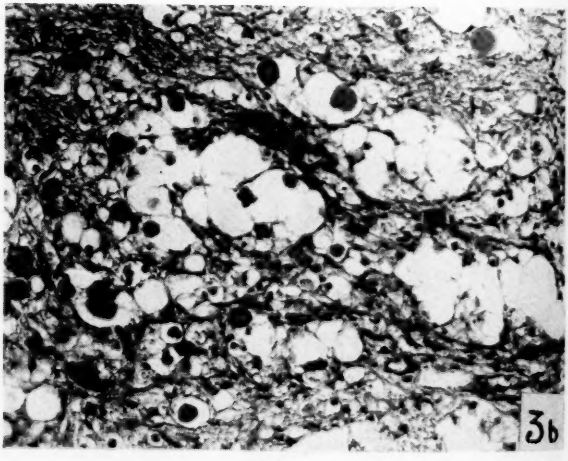
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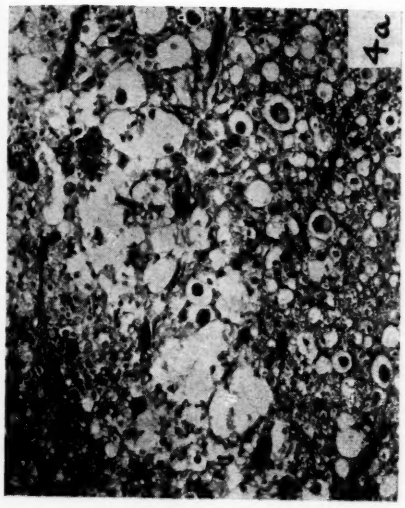
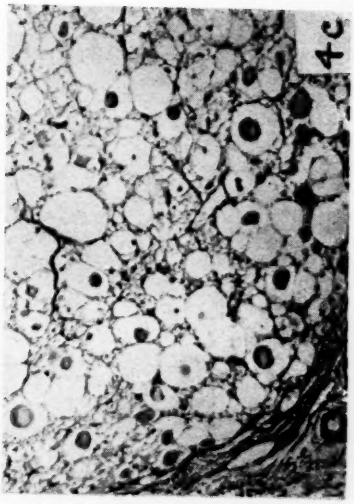
PLATE III





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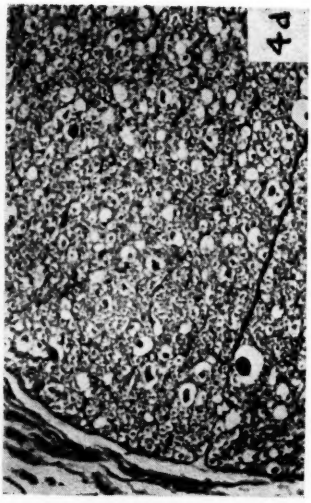


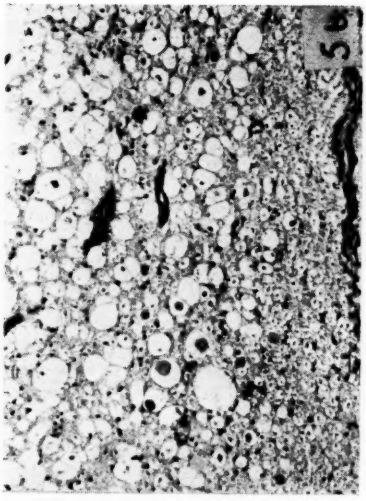
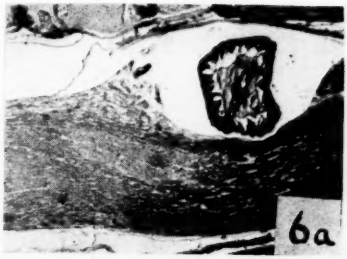
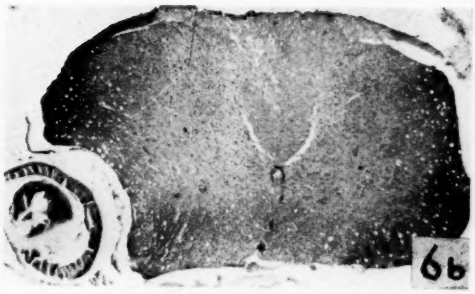


PLATE V





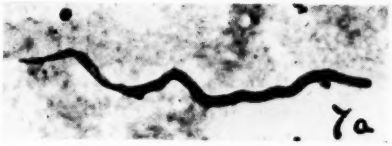
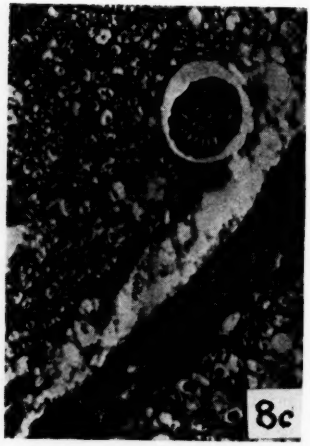
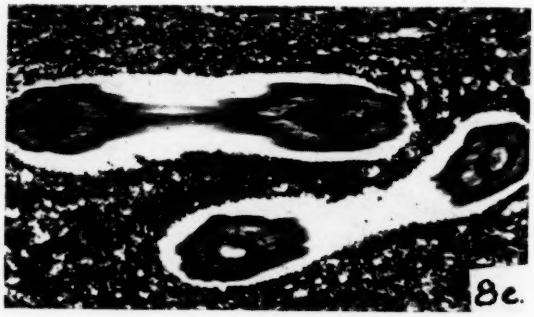
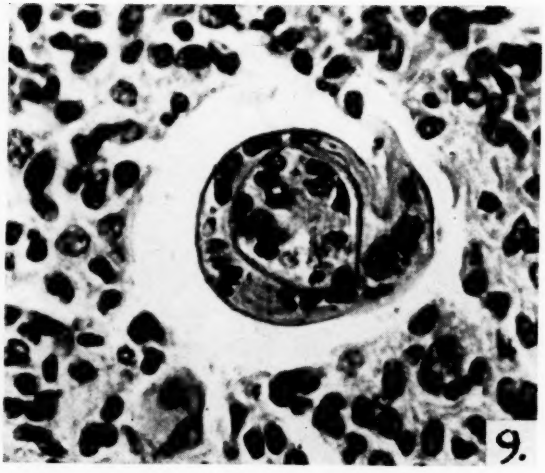


PLATE VI







Microfilariæ produced by the female (*Setaria digitata*) invade the blood of cattle and are transmitted in the mosquito season by insect vectors to fresh natural hosts (cattle), in which animals, neither in the Orient nor elsewhere, have there been any records so far of the occurrence of nervous disease. The Korean report indicates that the insect vectors for setariasis in sheep and goats are *Anopheles sinensis,** *Armigeres obturbans** (Niimi—Korean Commission), and *Aëdes togoi** has also been shown by Itagaki to be concerned with transmission of the equine paralysis. The filarid larvæ require about two weeks in the mosquito before becoming infective, and reaching the salivary glands (Fig. 8 *a*). Subsequent to the transfer of these mosquito-stage larvæ by the mosquitoes into the unnatural hosts, it has been estimated by the Japanese that there is a latent period of about one month before the appearance of neurological signs in affected animals. (Microfilariæ of *Setaria digitata* do not appear in the blood in *unnatural hosts*.) They noticed this incubation period particularly in Corriedale sheep *imported* into Korea from Australia, and it has been confirmed repeatedly in their experimental work, although the range of time has been variable, e.g., in some experimental horses from 15 to 66 days (Itagaki) and in experimental goat kids 15 to 33 days (Ishii). This is an important feature relating to the possible occurrence of the disease elsewhere (in man or animals), for signs might not be apparent until winter in temperate zones, if man or animals were bitten by the vectors in the late autumn. The path taken by mosquito-stage larvæ from the cutaneous mosquito inoculation is unknown, but they leave no trace before they emerge in the cranio-vertebral cavity to penetrate the meninges and nervous substance and produce malacia. The visible neural damage has been described, and it was intimated that in many cases the lesion itself might be difficult to find. The relationship between the presence of the nematode cause and neurological effect was established indisputably by the Japanese (first suggested by Fujita and later developed by Niimi and Shoho) in all the affected species—yet there were (and are still) difficulties. In many cases where parasites were found, one was usually present and only rarely two or more. Like many filarial worms, they have great tissue-wandering propensities. The parasite may not be found in the actual focus of softening, for it may travel out subsequent to the trauma and thus may be found at autopsy free in the cranio-vertebral canal. In the search for immature worms, therefore, Niimi originally filtered cerebrospinal fluid through gauze as part of his technique. Further, and of the utmost significance, he also found in some cases that the worms left the nervous system *after* the brain and cord were placed in fixative, and might be found *in the latter*. In one series parasites were found in the nervous system in 54 cases out of 176 sheep, and by using all techniques they were found in 44 per cent of cases in another. To the problem of detection of the lesion in the nervous system, there is thus added that of finding the causal parasite, and success in this is bound up with the duration of the disease. It is reiterated by the Japanese that, for the most fruitful search for the parasite in the nervous system, cases should be chosen in

* Reputed also to be vectors of Japanese *B. encephalitis*.

which the disease has been acute in onset and of a few days' duration. In cases kept to follow the clinical course (and they may linger for a few weeks), worms may not be found, for they may wander away, die and calcify, or disintegrate, and only fragments of a hyaline capsule may be found. The absolute identification of immature worms as nematode parasites is then difficult, as Fig. 9 shows (cf. also the same difficulties by Wilder [1950] in human nematode endophthalmitis). Typical nervous lesions are shown (Fig. 8 *b-d*), in which the parasites can be identified by the hyaline capsule and by the alimentary structure.

In the disease of goats in Ceylon (at the instigation of the authors), the association of immature nematodes with malacic lesions has now been established by McGaughey (1951). All the other evidence indicates we are dealing with an identical disease process: (*a*) the annual seasonal incidence coinciding with the mosquito season; (*b*) the clinical signs of dramatically acute or subacute paralysis; (*c*) the absence of constitutional symptoms or those indicative of infectious encephalitis; (*d*) the negative results obtained (by Crawford) in attempts to define micro-organismal or other causes; and (*e*) most important of all, the nature of the pathological lesion would seem to remove all doubt. (All cases sent from Ceylon to J.R.M.I. for pathological study were mature paralytic cases of many days' duration [except one of three days']; when these were examined the possibility of parasites being found in the CSF or in the fixative was unknown.) It would seem to be a matter only of time and care in study until the cause of lumbar paralysis in Ceylon—immature *Setaria digitata*—is confirmed experimentally. In this connection it may be recalled that, more than 50 years ago in India, young nematodes — *Setaria cervi* (synonym *S. digitata*) — were found in the nervous system in so-called equine paraplegia (Kumri). No real pathological examinations of these cases were ever made, and the worms were regarded as accidental invaders, perhaps transferred there by the hands of the prosector after death.

In substance this story of a parasitic ætiology of a nervous disease opens a fresh chapter in helminthic pathology. There have been many reports of the occurrence of a variety of helminths being found, on rare occasions, in the human and animal nervous system, and associated with neurological signs. (The specific disease known as Gid in sheep, caused by the presence of *Cœnurus cerebralis* in the brain [known for more than a century], is not in this category, for the sheep is the natural intermediate host of *Tænia multiceps*.) This condition described, however, would seem to represent an entity caused by the invasion of immature nematodes into the body of *unnatural hosts** (sheep, goats, and horses), in which they behave in an unnatural way in being strangely attracted (at least in small numbers) to invade and damage the nervous system.

* Although *neural setariasis* has not been found in cattle, it might theoretically be expected that *Setaria equina* (natural host, horse) might similarly produce nervous disease in the bovine species. Yet there is complexity here, for Shoho (1951) believes that intra-uterine infection by *Setaria digitata* may occur in cattle and produce so-called blindness and paralysis in new-born calves (2 cases with cerebellar lesions have been found); the unborn calf might thus be regarded as an unnatural host. Microfilariæ have been found in the blood of 2-to-3-month-old calves in Japan, which might also indicate intra-uterine infection. One of Olafson's cases of wobblers in foals was 5 days old!

XUM

Apart from this direct evidence, there is some relevant experimental work which supports the view that the nervous system may be a favourable anatomical site for parasites in unnatural hosts. Von Brand and Cullinan (1943) transplanted larval *Eustrongylides*—taken from fish in which they reside in cysts in liver, mesenteric fat, peritoneum, and muscles (adult-stage natural hosts being birds)—into subcutaneous pockets of chickens and rats; in both species, within 24 hours to 3 days, the larvæ invaded the nervous system, and paralysed and killed many of the experimental unnatural hosts (see Fig. 6 *a* and *b*).

[Steward (1935) demonstrated the role of another filarial worm, *Onchocerca cervicalis*, in the ætiology of a disease of the *Ligamentum nuchæ* of horses, in which the adult worms were often associated with *Brucella abortus*. Steward showed that the microfilariæ developed in the bloodsucking midge, *Culicoides nubeculosis*. The ecology of the parasite and its intermediate host afforded explanations of the previously unexplained vagaries in the distribution and incidence of equine fistulous withers and poll-evil. It is also of related interest that another species of *Onchocerca* (*O. volvulus*) is of pathogenic importance in man—in tropical African blindness associated with microfilariæ in the eye (see also later reference to work of Wilder).]

Experimental Cerebro-spinal Nematodiasis

The disease has now been reproduced by the Japanese in all species involved spontaneously, and a very few excerpts of results are given to indicate the ground which has been covered (see Korean Report). Microfilariæ of *S. digitata* live in the blood of cattle a long time, but were found to be incapable of producing the disease by intracerebral inoculation of infected blood into sheep.

In 22 experimental sheep, kept in a wire-gauzed compound, 10 were inoculated subcutaneously with 100 already matured larvæ harvested from the mosquito vectors after 14 days. Twelve animals were kept as controls. After one month 8 cases showed paralytic symptoms and 3 of these died; after two months all the remainder were killed; typical malacic lesions were found in all animals and in 4 of these, immature larvæ of *Setaria digitata* were found in the lesions. There was no contagion from sheep to sheep, infection being only by injection of sheep with mosquito-stage larvæ, and comparable experiments with the larvæ of *Setaria marshalli* were negative. The 12 control animals remained healthy.

In one experiment by Itagaki and his pupils (1947) in Japan, 8 horses were used, 6 being infected with mosquito-stage larvæ of *S. digitata* and 2 with those of *S. equina*. Typical symptoms and lesions with parasites were found in the first 6, but not in the latter 2. The incubation period ranged from 16 to 66 days and the approximate number of mosquito-stage larvæ injected varied from 132 to 357. In 3 experimental goat kids subcutaneously inoculated with 300 mosquito-stage larvæ (*S. digitata*), the onset of paralysis was 15, 22, and 33 days (Ishii, 1951).

In summary it would appear that the cycle of investigation regarding proof of the cause of this strange disease—now called *epizoötic* cerebro-spinal

nematodiasis) and known for more than 30 years in the Orient—has been completed, starting with the method of direct observation and finishing with that of experimental biology. Viewed as a whole, one of us (J.R.M.I.) regards the totality of the Japanese studies as a remarkable achievement, and one which in time will rank high, not only in the history of veterinary pathology but also in the history of *helminthic disease*.

Does the Disease Occur in Animals in Other Parts of the World?

Before embarking on speculation, we wish to be absolved from any suspicion of suggesting that here is an answer to all unsolved nervous diseases. In view of our own observations, however, there is no harm in mentioning some of our convictions, meant only as leads to follow.

That nematodiasis of the nervous system has not been considered before in connection with some paralytic disorders of animals is not astonishing—in view of the meticulous examinations of the nervous system required for identification of lesions and then of parasites. In many countries the occurrence of animal viral encephalitides may have overshadowed all other nervous diseases, and when the value of clinical diagnosis has been over-estimated, then doubtless all paralysed animals would be so regarded. In Japan, the disease was confused with virus encephalitis for years, and still may be so (there and elsewhere) if reliance is placed on clinical findings and neutralisation tests, as the latter may be positive even in the presence of a concomitant nematodiasis. The possible occurrence of dual infections (virus infection and worms) also must not be forgotten.

As an opening gambit it is manifest that nematodiasis must remain as a disease possibly occurring in animals in parts of the world: (*a*) where cattle carrying *Setaria digitata* exist as natural hosts; (*b*) where suitable insect vectors (mosquitoes, also *Stomoxys*) abound in the proper season; and (*c*) where other animals can act as unnatural hosts. With these circumstances in mind then the possibilities become immense. *Setaria digitata* is known to infect *bovidæ* and *cervidæ* as natural hosts in America, in some parts of Europe at least, in India, and nearly all regions of the Orient. In the Far East, therefore, it would seem unlikely for the disease to be confined only to Korea on the Asiatic mainland (and not China, Siam, Assam, or Burma), and only Ceylon and Japan as islands. In India there have been repeated references to an acute, or subacute, paralysis of goats in the Annual Reports of the Mukteswar Laboratories since about 1932. Unfortunately, the pathological descriptions do not suffice to depict the exact nature of the disease and the cause has not been found. Crawford also related (to one of us—J.R.M.I.) that he had observed two cases of lumbar paralysis in goats in a dealer's yard in Karachi. Delpy and Kaweh (1937) indicated that an enzoötic paralysis in goats had existed in Iran, although there is also a lack of good pathological data. Reference has been made to Kumri (in horses) in India, traditionally associated with "worm-(or snake)-in-the-eye" (immature adults of *Setaria cervi*, synonym *S. digitata*). Some Kumri cases have been reported to suffer from posterior paraplegia, and many years ago larvæ of *Setaria* were found in some cases in the vertebral canal. There is also little which is

accurately pathological to define the nature of Kumri, yet Hutyra and Marek (1949) mentioned a worker named Place finding hyperæmic areas of *softening* in the spinal cord. Kumri has also been reported in Burma (see Rippon, 1941). The observations of Kingston (1948) on paralysis of horses in Assam are also reminiscent of nematodiasis. In all these articles mentioned, good pathological studies might have given a clue to the cause but have been notorious by their absence.

Schwangart (1940) described an enzoötic paralysis of wild deer in south Germany, which had been known to hunters (and others) before the turn of the century. However, the author (a zoologist) was more concerned with the parasite than the disease, and the clinical descriptions are brief and there are no pathological comments which help. This paralysis was ascribed to adult worms (*Setaria labiato-papillosa* = *S. digitata, S. cervi*) found in the spinal canal. It is thus of interest to bring into line some observations by Monlux (1951) who has found a paralytic disease of deer in Texas. In one case (sections shown to one of us—J.R.M.I.) a solitary, hæmorrhagic malacic focus was found in the spinal cord (about c. 5), involving both grey and white matter; this lesion could not be distinguished from that described, but without the presence of a nematode.

Although it is not stressed in textbooks, *Setaria digitata* is known to be a common nematode infesting cattle in the U.S.A. (Dikmans—private communication), in which it is said to be non-pathogenic. Hence, in the face of these circumstances we might expect nematodiasis to be discovered sooner or later in appropriate agricultural regions of North America. We might then recall the paper by Olafson (1942) on so-called wobblers of foals in the U.S.A. From the clinical aspects and history given by Olafson (and a ciné-film of a case shown and described to one of us by Col. T. C. Jones, Veterinary Corps, U.S. Army) there seems some similarity to nematodiasis of *young horses* in Japan. The American disease affects young horses with posterior motor weakness and inco-ordination, rather than true paralysis, which might be concomitant with a solitary myelitic focus in the lower cord such as described by us. Olafson tentatively compared wobblers with swayback in lambs, but the bilateral, demyelinating or cavitating cerebral lesion of swayback has never been found in wobblers. There has apparently been no recorded, exhaustive pathological examination of the nervous system in wobblers—as was so necessary in nematodiasis—hence we do not know whether focal myelomalacia occurs. Circumstantial data might point to a consideration of helminths being involved in the cause of wobblers, for no other cause has been proved and the disease is not apparently a viral encephalomyelitis. (Through the courtesy of Col. T. C. Jones, some sections of spinal cord from wobblers were examined and, as he pointed out, an eosinophilic, partly hæmorrhagic meningitis, plus some secondary degeneration, was present.)*

* Olafson describes and illustrates hæmorrhagic foci in the spinal cord, and in his Figs. 4 and 5 it is evident that there are dilated (liquefied myelin sheaths) spaces around huge swollen axis cylinders identical with the picture seen in nematodiasis in areas away from the central malacic focus.

A peculiar nervous disease of unknown cause has been observed by Jensen and Bracken (1950) in Colorado, in cattle turned out on swampy pastures. From information privately received from Dr. Jensen, it seems there might be some points of resemblance to that described. There was acute onset, on fever, anorexia, inco-ordination, prostration, coma and sometimes blindness. One of us (J.R.M.I.) was privileged to view coloured photos of the anatomical lesions noted by Jensen—mainly hæmorrhagic malacic foci in the thalamus and cerebral cortex. This appearance is almost duplicated in some of the Japanese illustrations of the disease in sheep, and they also record that the thalamus might be a favoured site. A few typical sections were also examined, and revealed no essential differences in the lesions to those in goats from Ceylon, or in animals from Japan and Korea. This similarity in character of pathological changes thus repeatedly crops up in different species in many parts of the world, and we believe this must be of some ætiological significance—in spite of the fact, now almost a cliché, that the reaction of the brain is limited.

Reference might also be made to the encephalitis (often apparently discretely focal) of wild moose recorded by Fenstermacher and Jellison (1933), and by King (1939). There is some similarity in the recorded seasonal tendency, the inco-ordination and impaired vision—although we realise these signs could be duplicated in nervous diseases with different causes. Both authors thought that there might be more than one entity involved, yet all evidence pointed away from infection; the descriptions of the lesions are not remotely different from those of nematodiasis. In both the moose and Colorado cattle paralysis, in considering the possible role of *Setaria,* one must not be too rigidly impressed by the necessity for cases to occur in summer and autumn, for animals bitten by the mosquito vector in very late autumn might not show neurological signs until the winter. (In some experimental horses of Itagaki there was a latent period of 66 days.)

The medical implications are out of place in this paper. We raise elsewhere the question whether any form of nematode neuroparalysis may have existed in man (Orient or elsewhere), and has evaded recognition for the same reasons given in the case of domestic animals. It was previously pointed out (Innes, 1951) that in the pathological literature at least there are descriptions of necrotising myelitis, multiple degenerative softenings, or eosinophilic meningitis with focal malacia as well, and so on, which could bear scanning with nematodiasis in mind. (There is now a record with a direct human analogy to equine " worm-in-the-eye," by Wilder [1950].) In 46 eyes from children and adolescents (from many different parts of the U.S.A.), received over a period of years at the Armed Forces Institute of Pathology in Washington, D.C., a variety of diagnoses had been made; all showed some feature of eosinophilic, or granulomatous, endophthalmitis, but in none of the original sections cut were any worms found. Based on the resemblance of these lesions to some animal ones with a helminthic cause (originally suggested by Col. T. C. Jones, head of the Registry of Veterinary Pathology, Armed Forces Institute of Pathology), a re-examination of all the material was made by serial sectioning. Nematode larvæ

were then found in 24 eyes, and in the remainder the lesions were so uniform in type as to justify a diagnosis of nematode endophthalmitis for all. It is noteworthy that Wilder examined *2,300 sections from one eye* before finding a single larva (cf. the similar difficulty in finding immature forms in animal nematodiasis). Although uncertain of the exact species of nematode, it was considered they might be third-stage hookworm larvæ. Wilder concluded that nematodes might play a hitherto unrecognised role in blindness in children (cf. blindness in calves in Japan), particularly in the production of pseudoglioma and Coat's disease. Consequently, one might equally expect the occurrence of intracranio-vertebral, as well as intra-ocular, nematodiasis in human beings.

Conclusions and Summary

We reiterate our desire to be absolved of any accusation of making too far-fetched claims about the importance of nematodiasis. The facts as presented speak for themselves. Firstly, a "new," seasonal, paralytic disease of goats, sheep and horses was identified by the Japanese workers (first by Niimi and Kimura, although the original idea of parasitic cause was that of Fujita, and the first description of the disease in goats was by Emoto) to be based on a focal type of encephalomyelomalacia, affecting diverse parts of the nervous system in different cases. The cause, in our belief, has now been proved by Japanese workers beyond dispute to be linked with the invasion of the brain or cord (of these animals in Korea and Japan) by immature *Setaria digitata,* which inflict traumatic malacic damage with ensuing inflammation wherever they strike nervous substance. The traumatic concept is consistent with our pathological findings in experimental needle-trauma of the spinal cord in a sheep, and also with those in compression myelopathy (in animals and man). The type of lesion and its haphazard location is also in line with the neurological signs of a dramatically sudden (or subacute) paralysis. The Japanese disease has its identical clinico-pathological counterpart in the seasonal paralysis of goats in Ceylon.

The disease arises by the invasion of nematodes into unnatural hosts, and there is experimental evidence to support the idea that the nervous system is a tissue of special attraction for parasites when this eventuates. The requisite pathological examination of suspected cases might be a laborious one, in the sense of the number of blocks which might be required to be cut for detection of the lesion and then identification of young nematodes; yet unless this is done false ideas might be acquired and the cause never ascertained (cf. also the difficulties in human nematode endophthalmitis, by Wilder). Some reference is made to paralytic conditions in animals not yet fully investigated, which have been reported from many other parts of the world besides the Orient, in which the existing data suggest at least the need for a search into a possible nematodal cause (e.g., wobblers in horses in the U.S.A.). The most that we might be accused of in this connection is simply a pleading to veterinary pathologists to make more thorough examinations of the nervous system of any paralysed animal in the first place. Indeed, if this had been done in the past more would be

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known about the nature (and possibly cause) of all nervous diseases referred to in this report. Skin tests using *Setaria* antigen, and complement fixation tests, might be employed usefully as diagnostic aids.) Finally, we might mention that with establishment of the existence of the disease, then the means of control may lie at hand. Japanese workers (see Shoho, 1952) have already obtained some indications that the anthelminthic (diethylcarbamyl-4-methylpiperazine), may have some value as a prophylactic in the insect vector season, and as a curative when given at the *very early onset* of nervous signs.

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ACTINOMYCOSIS IN CARNIVORES:

A Review of the Literature

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In a recent clinical communication (Bader, 1949) it was remarked that a review of the literature on canine actinomycosis gave little information, and that the condition appeared to be rare. The first statement would appear to be true, as even the most recent textbooks do not provide detailed, comprehensive reviews. Within recent years, however, several authors (Mangrulkar, 1938; Brion, 1939; Gray and Hoeben, 1941; and Ginsberg and Little, 1948) have surveyed the literature and have described cases within their own experience. The number of cases described by these authors and others is only 45 to 50, but it is probable that many more have been noted but not recorded, and that still more have escaped notice.

In the chapter on actinomycosis in Henrici's "Molds, Yeasts and Actinomycetes," 2nd Edition, 1945, Emmons remarks that the subject of actinomycosis is difficult to present in a logical manner because of the large numbers of types of pathogenic actinomycetes and the multiplicity of diseases they cause on the one hand, and of errors in identification on the other. Our knowledge of the ætiology and pathology of many conditions in the larger domestic animals formerly grouped under the term "actinomycosis" was clarified by the work of Lignieres and Spitz (1902), Bosworth (1923), and Magnusson (1928). These workers differentiated actinobacillosis (infection with *Actinobacillus ligniersi*), chronic staphylococcal infection and chronic localised infections with other organisms, such as Corynebacteria, from infection with an organism similar to, if not identical with, *Streptothrix israeli* found in human actinomycosis. Recent comprehensive reviews of the literature on human actinomycosis have been published by Cope (1938), Rosebury (1944), and Conant and Rosebury (1948).

Until recently, little attention has been paid to actinomycosis in carnivores. The reason may be that the condition is rare in these animals, or it may be, as Brion (1939) says, that veterinarians tend to regard actinomycosis as almost exclusively a disease of bovine animals; in his detailed and extensive review, which, strangely enough, appears to have been overlooked by recent authors, he notes that most of the textbooks on veterinary pathology avoid the use of the term "actinomycosis" in dealing with dogs and cats, and seem to prefer such terms as "streptothricosis," "nocardiosis," "oosporosis," and "mycetoma."

Brion (1939) states that in the dog and cat, as in other animals, there is no special localisation of the infection, and that the disease may appear as a suppurative inflammation in any tissue, conjunctiva, subcutaneous connective tissue, bone, serous membranes, lungs, brain, uterus and mammary gland. The cases recorded in the literature and those in his own experience may be classified under the headings: (1) Cutaneous or subcutaneous; (2) serous membranes;

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(3) pulmonary; (4) central nervous system; (5) bone; (6) diverse types, usually granulomata or mycetomata.

Cutaneous or subcutaneous actinomycosis, apparently, is much the commonest type; according to Brion he has observed so many cases that he has had to refrain from recording them in detail. In addition to this unknown number observed by Brion, there are records, scattered through the literature from 1882 on, of 11 cases in dogs and one in a cat. The cases recorded more recently by Fethers (1934), Mangrulkar (1938), Ginsberg and Little (1948), and McGaughey, Bateman and Mackenzie (1951) may be classified as cutaneous and subcutaneous infection with extension to serous membranes.

Infection apparently confined to the pleural, peritoneal and other serous membranes has been recorded in nine dogs and six cats.

Pulmonary actinomycosis appears to be uncommon and actinomycotic encephalitis or meningo-encephalitis is rarer still, with only two cases on record.

Recently, the present writer has seen two cases of actinomycotic granuloma originating in a *Spirocerca lupi* nodule on the œsophagus; the granuloma had spread to the contiguous dorsal vertebræ and thence to the dura mater of the spinal cord, causing compression of the cord; these cases are reported in a later communication (McGaughey, 1952).

Actinomycotic osteitis in a dog was observed by Vachetta (1882), this being the first record of any form of actinomycosis in the dog; another case in a dog, but with little detail, was recorded by Fumagalli (1903), and two cases in cats are recorded by Brion (1939) himself. As for the diverse types, usually granulomata or mycetomata, to the four cases in dogs and one in a cat reviewed by Brion, there may be added two others described by Sheather (1932) and by Feldman and Mann (1932), Ginsberg and Little (1948), Forsyth (1949) and White (1939). Thus since 1882 there have been recorded only about 45-50 cases of actinomyces infection in dogs and 15 in cats but it is possible as suggested by Ginsberg and Little (1948) that it is much more common than these figures indicate.

The clinical signs of the cutaneous and subcutaneous infection are given in detail by Brion. He states that abscesses or extensive phlegmonous swellings with multiple fistulæ discharging granular pus are seen especially on the limbs and sometimes about the ears, neck, abdomen and tail. This type of infection is seen more often in the cat and he has noticed that the abscesses usually are in the parts more exposed to injury in fighting. The abscess develops slowly, the affected region becomes hot, painful and swollen. Soft hairless elevations are seen, the skin becomes eroded and pus is discharged.

The pus is sometimes grey but nearly always red or rose coloured as it contains some blood or blood pigment; it is not very thick and is full of small granules from a fraction of a millimeter to 2 mm., white, yellowish, rose, red or brown in colour and tending to sink to the bottom of the vessel in which the pus is collected. Brion recommends that, in order to detect and examine the granule the pus should be diluted with normal serum; after some seconds, the supernatant should be decanted and fresh serum added. If this is repeated

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several times the granules are freed of cellular debris and may be examined in the unstained state under a coverslip on a slide or spread on a slide and stained by Gram's method.

Brion noted that in areas where there was a well-developed aponeurosis the infection tended to remain localised, but in other less protected regions it spread between muscles. He also noted that while the regional lymphatic glands became swollen, hot and painful, they did not suppurate and he concluded that the organism was destroyed by macrophages. Abscesses occurring near joints cause great pain and lameness. The prognosis must always be grave but there are instances where surgical treatment leads to recovery.

He has not had very promising results with iodine therapy. Here one might refer to the interesting observations of Gray and Hoeben (1941) who observed and treated actinomycosis in four greyhounds. These authors noticed that the infection appeared in wounds cause by bites of other dogs; the wounds usually failed to heal in spite of first aid measures and later surgical treatment.

Their description of the progress of infection and of the pus is similar to that of Brion.

Ætiology: Almost all the authors who have recorded cases of actinomycosis in canines have described the typical granules found in the pus. Most of the descriptions agree with Brion's who states that " a typical granule has a central zone of small, coccoid bodies, probably spores, and an outer zone composed of filaments; all the bacterial elements stain Gram-positive but the tissue cell debris stains with the red counter stain." Brion says that he never has found acid-fast forms and that the granules are not calcareous, in contrast to those of bovine actinomycosis. In stained smears of crushed granules great pleomorphism is observed, filaments of varying dimensions, often showing dichotomous branching, short rod forms swollen at one end, small chains or masses of coccoid forms.

Cultural Characters: Those who are interested in the cultural characters of the various strains isolated from canine actinomycosis, should consult the publications of Brion (1939), Gray and Hoeben (1941), Emmons (1945), Skinner (1945), and Ginsberg and Little (1948).

Source of Infection: According to Skinner (1945), " the genus actinomyces is largely, if not exclusively, parasitic, living on tooth surfaces, in canine teeth and in tonsillar crypts of man and probably of lower animals, and causing infection under exceptional conditions."

The strict parasitism of *Actinomyces israeli,* the name given to the organism of human actinomycosis, has been demonstrated by various workers mentioned by Skinner. Similar investigations in animals would be desirable. The present author made cultures from swabs on the gums of four greyhounds; streptothrices resembling the organism isolated by Ginsberg and Little (1948) from their case No. 2 were easily recovered, especially if plates of alkaline blood agar *pH* 8.2 were used, but no micro-aerophilic strains were found.

It seems probable that the cutaneous and subcutaneous infection, and perhaps even those involving the deeper tissues, may result from bite wounds.

Treatment: Surgical interference, establishing drainage, should be carried

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out whenever possible. Brion (1939) states that he did not obtain much success with iodides, but Gray and Hoeben (1941) found that an extended course of sodium iodide in saline solution, 1 grain per lb. body-weight, given intravenously every three or four days, brought about good results in two of their cases. Ginsberg and Little (1948) obtained rapid and complete cure in one of their cases after the injection of two doses of 125,000 units of penicillin in oil. Penicillin has proved effective in many cases of human actinomycosis; in those which do not respond to penicillin, Coope (1949) advises the use of streptomycin or bacitracin.

Aureomycin has been used with excellent results in the treatment of cervico-facial actinomycosis in man by McVay and his colleagues (1950), and would seem to be the drug of choice where the owner is willing to meet the expense.

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ADDENDUM

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EFFECT OF SERA ON THE FERMENTATION REACTIONS OF *ERYSIPELOTHRIX RHUSIOPATHIÆ*

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Introduction

FOLLOWING the discovery, by Magendie[7] in 1846, of a starch splitting enzyme in serum, Hamburger[4] found that a maltase was also present. Since then it has been generally accepted that some, but not all, sera contain this enzyme.[1, 2, 6] In 1920, Tenbroek[11] pointed out that the presence of this enzyme would invalidate any positive results obtained in a carbohydrate fermentation test with maltose if serum had been added to obtain better growth. This is now acknowledged,[5, 10] but modern textbooks and reference books reflect the general disagreement as to which sera are free from maltase, and the temperature necessary to inactivate it.[8, 12]

Tenbroek[11] states that heating to 53 degrees C. for 1 hour, or 60 degrees C. for 15 minutes, was sufficient to inactivate the enzyme, but not 50 degrees C. for 15 minutes. Hendry[5] found that both 55 degrees C. for an hour and 55 degrees C. for 4 hours were ineffective, the enzyme only being destroyed at 65 degrees C. in 2 hours, at 75 degrees C. in 30 minutes, and at 100 degrees C. in 5 minutes. Rodrigues and Pacheco[10] heated the sera to 70 degrees C. for an unstated time to achieve inactivation, and Doxiades,[3] to 50 degrees C., also for an indefinite period.

Experimental

Methods.

The horse serum used was from a fresh batch from Messrs. Burroughs Wellcome & Co. The bovine serum was from old stock which had been stored at 4 degrees C. for twelve months and then Seitz filtered. The other sera were collected direct from the animals and used within two days.

The serum under test was added, 0.1 ml., to solutions of peptone water and maltose (5 per cent) in bottles containing 3 ml. of solution (giving a serum concentration of 3 per cent) prior to inoculation. The heated serum was prepared in bulk in a water bath and added to the peptone sugar solution when cool. A control containing the serum sugar solution, but uninoculated, was tested for sugar, by the formation of ozazone crystals, after incubation. A parallel series of peptone water and glucose was inoculated also, since *E. rhusiopathiæ* does

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not produce acid from glucose unless serum is added,[13] and it was not known if sera other than horse serum would be effective in this respect.

The bottles were inoculated with 0.1 ml. of an 18 hour broth culture of the twelve strains of *E. rhusiopathiæ* which had been used previously[13] (the inconsistent maltose fermentation results of which led to this investigation).

Results.

The results, Table 1, support the hypothesis of the presence of a maltase in horse, sheep, rat and mouse sera, and its absence in rabbit, guinea-pig, human, and, possibly, bovine sera. The doubt arising in the case of bovine serum is due to the age of the sample used, and Tenbroek's[11] statement that serum stored for 18 months at 4 degrees C. is still active, is unsupported.

Confirmation of this hypothesis is given by the results (Table 2) of the ozazones crystallised from the serum-sugar mixtures which had been incubated. In those cases where a maltase was suspected maltazone crystals were rare or absent, and in two cases (sheep and rat) both maltazone and glucazone crystals were obtained from a specimen previously containing maltose only.

The inactivation of this enzyme by heat (Table 3) was unsuccessful, since, in order to obtain destruction of the enzyme, the serum had to be heated until denatured, and under these conditions it failed to support the growth of *E. rhusiopathiæ* even in glucose medium. The claims of Tenbroek[11] and Doxiades[3] are, therefore, not confirmed, and the temperatures employed by Hendry[5] and Rodrigues, *et al.*[10] render the serum unsuitable for this purpose.

The effect of the type of serum on the growth of *E. rhusiopathiæ* in glucose medium, as judged by the speed of acid production and by macroscopic turbidity, was noticeable, human serum supporting little, and rabbit serum least, growth.

Summary

1. A maltase is present in horse, sheep, rat and mouse sera, possibly in bovine, but not in rabbit, guinea-pig or human sera.

2. The maltase is inactivated only by temperatures which destroy the beneficial effect of the serum upon the growth of *E. rhusiopathiæ*.

3. The growth of *E. rhusiopathiæ* is not increased to a uniform extent by sera from differing species.

4. The variable fermentation of maltose obtained previously was presumably due to a combination of the effects of the type of serum used and the presence of an enzyme. This cannot, therefore, be used as a differential reaction as suggested.

5. It is inadvisable to use any serum in a carbohydrate (maltose) fermentation test which has not been tested for its specific effect on the growth of the organism as well as for the presence of a maltase. For *E. rhusiopathiæ*, guinea-pig serum is probably the most favourable.

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TABLE 1.

Acid production from glucose and maltose by *E. rhusiopathiæ* in the presence of different sera.

Serum	Sugar	STRAIN 353	354	445	446	904	905	1061	1926	1927	1928	1929	2023
HORSE	Glucose	A	A	A	A	Sli A	A	Sli A	A	A	A	A	A
	Maltose	A	A	A	A	A	Sli A	Sli A	A	A	A	A	A
OX	Glucose	—	A	A	A	Sli A	Sli A	Sli A	A	A	Sli A	—	—
	Maltose	—	—	—	—	—	—	—	—	—	—	—	—
RABBIT	Glucose	Sli A	A	A	A	—	Sli A	—	Sli A	A	Sli A	—	—
	Maltose	—	—	—	—	—	—	—	—	—	—	—	—
G.-PIG	Glucose	A	A	A	A	A	A	A	A	A	A	A	A
	Maltose	—	—	—	—	—	—	—	—	—	—	—	—
RAT	Glucose	A	A	A	A	A	A	A	A	A	A	A	A
	Maltose	A	A	A	A	A	A	A	A	A	A	A	A
MOUSE	Glucose	A	A	A	A	A	A	A	A	A	A	A	A
	Maltose	A	A	A	A	A	A	A	A	A	A	A	A
SHEEP	Glucose	A	A	A	A	A	A	A	A	A	A	A	A
	Maltose	A	A	A	A	A	A	A	A	A	A	A	A
HUMAN	Glucose	A	A	A	A	A	A	A	A	A	A	A	A
	Maltose	—	—	—	—	—	—	—	—	—	—	—	—

TABLE 2.

Ozazone crystals obtained after addition of serum to maltose.

SERUM	OZAZONE CRYSTALS
Horse	Few maltazone.
Bovine	Maltazone.
Rabbit	Maltazone.
Guinea-pig	Maltazone.
Rat	Maltazone and Glucazone.
Mouse	None obtainable.
Sheep	Glucazone.
Human	Maltazone.

TABLE 3.

Effect of heated sera on fermentation reactions.

GLUCOSE	353	354	445	446	904	905	1061	1926	1927	1928	1929	2023
HORSE SERUM:												
Unheated ...	A	A	A	A	Sli A	A	Sli A	A	A	A	A	A
At 60 degrees C.	Sli A	A	A	Sli A	Sli A	Sli A	Sli A	Sli A	A	Sli A	Sli A	Sli A
At 65 degrees C.	Sli A	Sli A	A	Sli A	Sli A	Sli A	Sli A	Sli A	A	Sli A	Sli A	Sli A
BOVINE SERUM:												
Unheated ...	—	A	A	A	Sli A	Sli A	Sli A	A	A	Sli A	Sli A	—
At 60 degrees C.	—	A	A	Sli A	Sli A	Sli A	Sli A	A	Sli A	Sli A	Sli A	—
At 65 degrees C.	—	Sli A	A	Sli A	Sli A	Sli A	Sli A	Sli A	A	Sli A	—	—
MALTOSE HORSE SERUM:												
Unheated ...	A	A	A	A	A	Sli A	Sli A	A	A	A	A	A
At 60 degrees C.	Sli A	Sli A	—	A	Sli A	A	Sli A	Sli A	Sli A	Sli A	Sli A	Sli A
At 65 degrees C.	—	Sli A	—	Sli A	—	A	—	Sli A	—	—	—	—

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THE USE OF LAPINISED RINDERPEST VIRUS VACCINE to replace the annual inoculation of cattle previously protected with inactivated formolised spleen vaccine

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CHENG and Fischmann (1948) have recorded that lapinised rinderpest virus vaccine will protect the indigenous cattle of China, as well as imported dairy cattle, against natural rinderpest. Watson (1950 and 1951) has reported that dairy cattle imported into Hong Kong were protected by the vaccine, and that immunity lasted for at least one year. Laboratory experiments at Kabete and field trials in East Africa between 1948 and 1951 (Brotherston, 1951 *a*) have confirmed that the freeze-dried lapinised vaccine will immunise Zebu cattle, certain highly susceptible indigenous breeds, imported European cattle, as well as grade-crosses of these with African Zebu breeds; the immunity conferred lasted between nine months and fifteen months. Cattle injected with the vaccine resisted infection with virulent rinderpest virus when this was injected subcutaneously at 84 and 100 hours after vaccination. In an outbreak recorded by Brotherston (1951 *b*), involving a herd of 1,800 susceptible cattle, some of which were showing clinical symptoms of rinderpest, the use of lapinised vaccine controlled the disease with a reduced mortality of 3 per cent and prevented the extension of the outbreak to cattle on neighbouring farms.

As the lapinised vaccine was of low pathogenicity, causing no visible reactions in local and highly susceptible imported cattle, it was thought that

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the virus might not have sufficient invasive power to evoke immunity in stock with a low-grade or declining immunity. If this proved to be the case, it would be an obstacle to the change-over from inactivated tissue vaccine to lapinised virus vaccine, for the annual protection of susceptible grade and imported cattle, in Kenya. A field experiment was designed, to elucidate the following points :—

(a) The state of immunity in cattle inoculated over a year previously with formolin-inactivated rinderpest tissue vaccine.

(b) To determine if lapinised vaccine would superimpose an immunity on the residual immunity of cattle previously given formolin-inactivated spleen vaccine.

(c) To determine the state of immunity in cattle vaccinated with lapinised vaccine, at one year P.I. and to see if such cattle may be re-immunised with lapinised vaccine.

Parts (a) and (b) of the experiment are described in this paper. The first of Part (c) is described, and the final stage will be reported at a later date.

General Explanation.

A farm was chosen for the experiment where the cattle, which were all high-grade animals, had been protected with formolin-inactivated spleen vaccine as a routine measure, over a period of years. Stock at one year of age had been given a triple course of vaccine, irrespective of any previous anti-rinderpest prophylaxis, that is, 10 ml. of vaccine each week for three weeks; thereafter, all stock which had received the triple course were inoculated annually with a "booster" dose of 10 ml. of spleen vaccine.

The 27 cattle chosen for Parts (a) and (b) of the experiment were of the same age, and all of them had received the triple course of rinderpest vaccine in August, 1949; as animals under one year old, they had previously been given 10 ml. of the vaccine. At the time of the experiment, in October, 1950, these cattle were two months overdue for the annual reinforcement of immunity, and it seemed reasonable to assume that they had retained some immunity, but that it would be of a low grade. It was proposed to divide these cattle into two groups, in one of which the animals would be challenged with virulent bovine virus; cattle in the other group were to be vaccinated with lapinised vaccine and then similarly challenged.

The cattle chosen for Part (c) of the experiment were animals between eight and twelve months old, which were susceptible and which would normally have been protected by injection of 10 ml. of inactivated spleen vaccine, followed by a triple course when over one year old. It was proposed to vaccinate these cattle with lapinised vaccine, to challenge a representative number shortly afterwards to ensure that they were immune, and to leave the remainder for one year. At the end of that time the cattle were to be divided into two groups; the animals in one were to be challenged and the cattle in the other were to be vaccinated with lapinised vaccine and then similarly challenged.

The bovine rinderpest virus employed was the stock Kabete "O" strain, and the challenge was carried out at the laboratory by subcutaneous injection

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of the virulent virus. The lapinised virus vaccine employed was batch K 17, proved potent in cattle at a dose of 0.0002 g. and used at a dose of 0.004 g., given subcutaneously in 2 ml. of sterile normal saline. Cattle were vaccinated on the farm and groups identified by brand were removed to the laboratory and challenged at 25 days P.I.

Part (a) of the Experiment.

The state of immunity of cattle 14½ months after vaccination with formolised spleen vaccine.

Fourteen cattle which had previously received a triple course of formolin-inactivated spleen vaccine in August, 1949, were challenged on November 11, 1950. These animals were two months and 11 days overdue for the annual reinforcement of immunity. Table I shows the results of challenge at approximately 14½ months after the vaccination with formolin-inactivated spleen tissue.

TABLE I.

Cattle No.	Reaction to Challenge.	Result.
1139	Mild thermal reaction only. Survived.	Partially immune.
1140	" " " " "	" "
1152	" " " " "	" "
1141	Severe thermal reaction; killed for production of spleen vaccine.	Susceptible.
1142		"
1143		"
1144		"
1145		"
1146		"
1147		"
1148		"
1150		"
1151		"
1149	Died rinderpest day 7 P.I.	"

From the reactions of these cattle, it was concluded that three out of 14 had retained a low-grade immunity 14½ months after receiving a triple course of formolin-inactivated spleen vaccine.

Part (b) of the Experiment.

The revaccination with lapinised vaccine of cattle previously immunised with formolised spleen vaccine.

Thirteen cattle which had previously received a triple course of formolin-inactivated spleen vaccine in August, 1949, were given lapinised vaccine on October 17, 1950. They were then one month and 19 days overdue for the annual reinforcement of immunity. These animals were removed to the laboratory and challenged on November 11, 1950. Table II shows the results of challenge 25 days after injection with lapinised vaccine.

TABLE II.

Cattle No.	Reaction to Challenge.	Result.
1156	Mild thermal reaction only. Survived.	Partially immune.
1153	No reaction, no symptoms.	Immune.
1154	" " " "	"
1155	" " " "	"
1157	" " " "	"
1158	" " " "	"
1159	" " " "	"
1160	" " " "	"
1161	" " " "	"
1162	" " " "	"
1163	" " " "	"
1164	" " " "	"
1165	" " " "	"

From these results it was concluded that the majority of the cattle had received adequate protection from the injection of lapinised vaccine.

Part (c) of the Experiment.

The revaccination with lapinised vaccine of cattle previously immunised with lapinised vaccine.

First Stage.

Some 120 susceptible weaners between eight and twelve months of age were injected with lapinised virus vaccine. At 25 days P.I., ten were removed to the laboratory and challenged with virulent bovine virus. All cattle remained normal and proved immune except one, which died from East Coast fever; an unvaccinated control proved susceptible. It was concluded therefore, that all the cattle which received lapinised vaccine had a reasonable protection. It now remains to carry out the second stage of Part (c) of the experiment.

Conclusions from Parts (a) and (b).

It will be noted that 11 out of 14 of the test cattle protected with a triple course of formolin-inactivated spleen vaccine had lost their immunity at $14\frac{1}{2}$ months P.I. Cattle of a similar group when vaccinated at this time with lapinised virus vaccine acquired a serviceable immunity, as shown by challenge with virulent bovine virus.

Discussion.

The introduction into Kenya by Daubney (1928) of a formolin-inactivated rinderpest tissue vaccine, made possible a safe method of protecting highly susceptible grade cattle. In addition, as the vaccine could be used by the farmer himself, the Veterinary Field Services were saved considerable time and labour. However, inactivated tissue vaccines have several disadvantages; they are expensive to produce, a course of three inoculations each at a weekly interval is required before a solid immunity is induced, and the immunity is of short

duration and requires annual reinforcement. Because of the long time required for immunity to become serviceable, the method is of limited value in combating an outbreak of rinderpest. Nevertheless, it has proved excellent for the class of animal for which it was intended, and with the use of K.A.G. in Zebu stock, the two techniques have proved of inestimable value in the control of rinderpest.

Some of the advantages of lapinised virus over spleen vaccine are:—

(1) Vaccine prepared from the rabbit is cheap. One rabbit produces 500 to 600 cattle doses.

(2) It is possible to titrate accurately and quickly, in cattle, the antigenic properties of lapinised vaccine before issue.

(3) One injection only is required.

(4) The lapinised vaccine produces a very mild reaction which has no adverse effect on the milk yield, and no injurious effect on pregnant animals.

(5) The lapinised vaccine confers a rapid protection and may be used to combat outbreaks of rinderpest.

(6) Many thousands of doses may be packed into a small container.

It is true that the vaccine provokes little visible reaction, and induces a comparatively short immunity, but it is considered that these disadvantages are outweighed by the benefits. In view of the simplified method of immunisation, and as the vaccine appears to induce immunity under the circumstances described, it seems likely that lapinised virus vaccine will come to replace the formolin-inactivated rinderpest spleen vaccine to protect grade cattle against rinderpest. In the case of cattle previously immunised with inactivated rinderpest spleen vaccine, it appears that lapinised virus vaccine may be used to re-immunise these cattle at about 14 months after the former inoculation.

Acknowledgments.

We are indebted to Mr. D. Cole, of Cole Estate, Naro Moru, Kenya, for placing the cattle used in the experiment at our disposal. This paper is published by permission of the Director of Veterinary Services, Kenya, and the Director, East African Veterinary Research Organisation.

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REVIEWS

CIRCUS DOCTOR, by J. Y. Henderson, D.V.M., Chief Veterinary Surgeon of the Ringling Bros. and Barnum and Bailey Circus. London: Peter Davis. Price 12s. 6d.

ALL the world loves a circus, and the greatest fans are those most closely connected with it. This is a remarkable fact. If any reader should doubt, I

would ask him to stand discreetly near the entrance or exit to the sawdust ring. He will find that he is one of an audience of experts, all circus folk, watching the antics of fellow artistes with deep concentration and obvious enjoyment. What do circus folk do in their odd times of leisure? Why, they go to other circuses.

No community is so mixed or variegated, in no place is comradeship at a higher level, and in no other show does recognition of skill or art meet with more wholesome approbation, even when the performer be a rival.

Men and women of different race, colour and creed live together in close harmony and set an example to the rest of the world.

Dr. Henderson is no exception to the rule, " Once a circus man, always a circus man." He was inoculated by chance, but the virus has taken and produced such a reaction that the circus is in his blood for life.

His book is a tribute to the training given in our colleges, for it substantiates something of which we have been proud, i.e., the course of instruction in a recognised Veterinary School enables a man or woman of reasonable competence and common sense to turn his, or her, attention and with success to any type or variety of veterinary work.

The fundamental principles remain the same; it is environment which alters.

Any reader will find this book to be teeming with interest from start to finish. Veterinary surgeons will find information which they can put to good use should the occasion arise. They will read of the dire effects of internal parasites on bears, and how to avoid them. They will get new ideas on the treatment of laminitis, for Dr. Henderson appears to be able to incite resolution in almost every case. What a pity that his methods of treatment have come so late in the day. Thirty years ago laminitis was one of the most serious lesions in town studs, and there was ample evidence in the streets demonstrating our inability to cure.

The words on big cats and their management are welcome. The accounts of his surgical feats on these beasts show at once that he is a man of agility, resolution and courage.

The big cats are the bane of the circus " vet." The hazards are so great that there is little one can do as a rule. Often it is a case of " Patient, cure thyself." This rule is not valid in Ringling's Circus.

What extraordinary accidents occur in an American circus. Even the trained horses sometimes cavort about amongst the audience, not to mention the elephants and cats. Thank God the animals of the English circus are more rational in behaviour. Is the American air of a more stimulating nature?

Some of Dr. Henderson's experiences are a little beyond the factual comprehension of his English colleagues. They are great entertainment.

There is one story which will thrill and, indeed, may horrify the reader. I refer to the fire. Fire and snow are dreaded by circus folk. It says much for Ringling's and their employees that they showed such courage and resource in this calamity, and that, like all good troupers, come what may the show must go on. It opened again on the same evening.

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The circus is the highlight of all entertainment, its people are the cream of the earth, and I am sure that this book will have a wide appeal to the public and join the ranks of the " best-sellers."

DISEASES OF DOMESTIC ANIMALS IN AUSTRALIA. PART 2: FLY, LOUSE AND FLEA INFESTATIONS. Service Publication (Division of Veterinary Hygiene) No. 6: Commonwealth of Australia, Department of Health, Canberra, A.C.T. 173 pp., 16 plates, 18 maps, 13 tables, 2 figures.

THIS publication, which forms Part 2 of a series dealing with the diseases of domesticated animals in Australia, is issued under the ægis of the Division of Veterinary Hygiene, Commonwealth Department of Health. Its aim is not to provide information on the morphology and recognition of the various Australian arthropods, for such information is available in textbooks, but rather to state what flies, lice and fleas infest animals in the Commonwealth, in what areas they occur, and where they are sufficiently prevalent to cause ill-health. The circumstances under which the parasites affect the health of stock, particularly under Australian conditions, the effects of the arthropods on the animals, and the control measures are also discussed. With certain exceptions, symptoms and lesions are described only to the extent necessary to illustrate the effects under Australian conditions. The information about the life histories of the parasites has been compiled almost entirely from the published articles of Australian workers, and it is admitted that no attempt has been made to correlate this with the discoveries of workers in other parts of the world.

HUMAN BLOOD GROUPS AND INHERITANCE, by S. and L. F. Lawler. London: William Heinemann, Ltd. Price 3s. 6d.

IN one way or another, we are all interested in blood groups. As blood donors, we may like to know what happens to our blood before it is given to a patient, and as patients we may like to know how the tests that guard us against an incompatible transfusion are carried out. We may also, if we are married, be worried about the significance of the Rhesus factor and its role in the production of hæmolytic disease of the new-born, while as biologists we may be curious to see how knowledge of the inheritance of human blood groups can throw light on human genetics. The authors of this book have succeeded in placing before the non-expert reader a clear account of a specialised subject, and there is something to interest us as blood donors, patients, parents or biologists.

After a historical note, the method of testing for the various blood groups is outlined clearly. The various blood group systems are discussed, with particular reference to their incidence and inheritance—these are the A_1A_2BO, Rhesus, MNS, P, Kell, Lewis, Lutheran, Duffy, and Kidd systems, respectively. A chapter on the National Blood Transfusion Service traces what happens to the blood given by a donor, while the final chapter indicates how a knowledge of blood groups and of their inheritance and distribution may be not only of

practical use, as, for example, in controversial paternity cases, but also in a broader way in throwing light on various ethnological, anthropological and genetical problems in man. There is a useful short glossary and an index.

PARASITES OF DOMESTIC ANIMALS, by T. W. M. Cameron. Second edition. London: A. & C. Black, Ltd. Price 38s.

THE first edition of this textbook appeared in 1934 under the title of "The Internal Parasites of Domestic Animals." The bulk of the textual matter was devoted to helminthology, and there was a small section on protozoology. As the courses in parasitology taught in the British Veterinary Schools and elsewhere also include entomology there was a feeling of disappointment amongst students and teachers that this subject was not represented in the first edition. Professor Cameron has, however, remedied this state of affairs by including a section on the arthropods of veterinary importance in this second edition, as well as bringing up to date the information on protozoa and worms.

Part I of the book is a general introduction to parasitology, and includes sections dealing with nomenclature and the history of the subject. Part II concerns the protozoa, and now includes information on *Trichomonas* at the expense of the Sarcosporidia. Part III deals with the nematodes, acanthocephalids, trematodes and cestodes of veterinary importance, with a concluding section on the geographical distribution of the helminths. Part IV is devoted to immunity and serology, and shows considerable revision because there have been numerous additions to our knowledge of resistance to parasites during the past 10 to 15 years. Part V, on the therapeutics of helminth infections, has been brought up to date by the inclusion of notes on the newer drugs, such as sodium fluoride, phenothiazine, etc. Parts VI and VII deal with external parasites, the former with the leeches and the latter with the insects, ticks and mites, and although the account of the systematics and morphology is reduced to the bare minimum, this does not seriously detract from the usefulness of the information given. Part VIII is a new chapter added to the book, and concerns the principles of prevention of helminthic diseases. Here, Professor Cameron reviews and discusses the different control measures that may be adopted in an attempt to curb or banish worm infestations. Part IX treats of the various techniques applicable to parasitology, and the concluding Part X consists of host lists, diagrammatically arranged, and a recast bibliography.

Whilst the text is generally of a high order and maintains the lucid, descriptive style that was a feature of the first edition, the book is not without its faults and shows the lack of adequate care in proof-reading, and even in revision. For example, it is stated that *Trypanosoma congolense* is not transmissible to laboratory animals (p. 26), although it is well known to be infective to most laboratory rodents; contradictory statements about the number of sporocysts in *Eimeria* and *Isopora* occur on p. 34; *Leucocytozoon* is mis-spelt (p. 48); under *Strongyloides* (p. 62) the phrase, "Parasitic generation hermaphroditic (pathenogenic?) like female of *Trichostrongylus* (q.v.)," is most misleading; "cercariæ"

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(p. 168, line 10 from foot) should read " miracidia "; the specific names of some ticks are mis-spelt, e.g., *microphus* for *microplus* and *winthermi* for *winthemi* (p. 317), and *sinus* for *simus* (p. 321). Certain of the figures of mange mites redrawn from Highley's excellent illustrations in Hirst's pamphlet dealing with the mites injurious to domestic animals are inaccurate, e.g., Fig. 154, labelled *Notoedres* male, is really a modified copy of the male *Cnemidocoptes* drawing, but in which a sucker-bearing pedicel appears on one of the third pair of legs and not on the other. This lop-sidedness is evident in Fig. 156, in which the male nymph (but labelled female) of *Psoroptes* lacks a pedicel and sucker from one of the second pair of legs and the male lacks a pedicel and sucker from one of the third pair of legs, and in Fig. 158, in which the male *Otodectes* lacks a pedicel and sucker from one of the third pair of legs. The statement (p. 330) that Psoroptes male has suckers with segmented stalks on the first, second, third and fourth legs is incorrect. It is *Cnemidocoptes mutans* that burrows beneath the leg scales, and not *C. gallinæ*, which is found in the skin along the feather shafts in chickens (p. 330). *C. midus* (p. 331) should be *C. nudus*. It is to be regretted that, besides the Stoll dilution egg-counting technique, there is no mention of the Gordon-Whitlock egg-counting method.

If the reviewer has concentrated upon some of the deficiencies of this text-book, it is not without reason, because one of the responsibilities of a University teacher is to give advice to students about the books they should consult, and as this one is styled, " A manual for veterinary students and surgeons," the reviewer is reluctant in giving to it the whole-hearted support which it might otherwise merit.

PERSONAL

I AM completing a life of the painter George Stubbs (1724-1806) and a catalogue raisonné of his work. I should be grateful for information from those owning pictures and drawings by this artist who have not already assisted me. —Basil Taylor, 86c, Philbeach Gardens, London, S.W.5.

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